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| EXAMINER | |
|---|---|
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/572,987 | TIEN ET AL. | |
| | Examiner | Art Unit | |
| | NATHAN E. COMSTOCK | 4132 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *10,19,20,24,31,39,40,44 and 51-58* is/are pending in the application.

4a) Of the above claim(s) *31,39,40,44 and 55-58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10,19,20,24 and 51-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 March 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *03/23/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Election/Restrictions*

1. Restriction is required under 35 U.S.C. 121 and 372.

2. This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

3. In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

> Group I, claim(s) 10, 19-20, 24, and 51-54, drawn to three-dimensional hydrogel structures.
>
> Group II, claim(s) 31, 39-40, 44, and 55-58, drawn to methods for micropatterning three-dimensional hydrogel structures.

4. The inventions listed as Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Groups I and II share the common and/or corresponding technical features of a hydrogel structure micropatterned by a mold from which the hydrogel has been separated, the hydrogel structure comprising: a polymer array of a hydrogel, the polymer array comprising a fluid that hydrates the polymer array and a second hydrogel comprising a second polymer array hydrated by a second fluid and a micropattern defining a surface of at least one hydrogel the micropattern corresponding to an inverse micropattern transferred from a mold after separation of the mold from the hydrogels, wherein the hydrogel is interfaced with a precursor of a second hydrogel comprising a second polymer array hydrated by a second fluid, whereby the precursor of the second hydrogel diffuses into the

hydrogel interfaced therewith to adhere the hydrogels as the second hydrogel forms; whereby a destabilizer contacting the hydrogel and the second hydrogel conforms at least one of the hydrogels to adhere the interfaced hydrogels together when a concentration of the destabilizer is reduced, whereby precursors of the hydrogel and the second hydrogel were combined to interface the hydrogels as at least one hydrogel is formed.

5. However, in order to be considered a common special technical feature, any such feature must be novel and non-obvious. The above described technical features are not novel and non-obvious. U.S. Pat. No. 6,479,072 to Morgan et al. discloses a hydrogel structure (composite dermal analog, col. 10, lines 33-48) micropatterned by a mold (PDMS negative replicate, col. 9, lines 62 to col.10, line 4) from which the hydrogel (basal lamina analog, col. 9, line 40 to col. 10, line 59) has been separated (dried membrane is peeled from PDMS replicate, col. 9, lines 62 to col.10, line 4), the hydrogel structure comprising: a polymer array of a hydrogel (cross-linked collagen-GAG dispersion, col. 9, lines 40-62 and col. 10, lines 49-59), the polymer array comprising a fluid that hydrates the polymer array (water/phosphate buffered saline, col. 10, lines 49-59) and a second hydrogel (rehydrated collagen sponge, col. 10, lines 33-59) comprising a second polymer array (cross-linked collagen-GAG dispersion, col. 10, lines 33-59) hydrated by a second fluid (water/phosphate buffered saline, col. 10, lines 49-59) and a micropattern (channels 42, col. 10, lines 5-8) defining a surface of at least one hydrogel (col. 10, lines 5-8) the micropattern corresponding to an inverse micropattern transferred from a mold after separation of the mold from the hydrogels (col. 9, lines 63 to col. 10, line 8), wherein the hydrogel is interfaced with a precursor of the second hydrogel (uncrosslinked collagen-GAG dispersion, col. 10, lines 33-48), whereby the precursor of the second hydrogel diffuses into the hydrogel

interfaced therewith to adhere the hydrogels as the second hydrogel forms (at least a limited amount of diffusion of a dispersed component would inherently occur where the microfabricated basal analog is floated on the dispersion, because the basal analog is porous and not hydrophobic (it can be hydrated by a dilute acetic acid solution, col. 10, lines 49-59)).

6. Morgan does not explicitly disclose that a destabilizer contacting the hydrogel and the second hydrogel conforms at least one of the hydrogels to adhere the interfaced hydrogels together when a concentration of the destabilizer is reduced, or precursors of the hydrogel and the second hydrogel were combined to interface the hydrogels as at least one hydrogel is formed.

7. However, these limitations are product-by-process limitations. Even though product-by-process claims are limited by and defined by the process, determination of patentability (and hence whether the limitations are novel and possess inventive step) is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. See In Re Thorpe, 227 USPQ 964. See MPEP 2113. Absent a showing to the contrary, it is expected that this specific method of adhering or interfacing the hydrogels does not confer any structural or compositional limitations to the claimed article beyond the limitations elsewhere recited as common technical features of the claims and anticipated by Morgan. There is currently no indication that any different structure would result in the three-dimensional hydrogel structure because the hydrogels were interfaced through the use of a destabilizer to destabilize one of the hydrogels (i.e. causing it to de-gel) and then removing the destabilizer (i.e. allowing the hydrogels to re-gel) as opposed to simply causing one hydrogel to gel while already interfaced

with the other hydrogel, especially since the character of a de-gelled hydrogel and an ungelled hydrogel precursor would essentially be the same with regard to forming an interface with another gel, as taught by Morgan (col. 10, lines 33-59). There is likewise no indication that that interfacing the precursors of the hydrogels would lead to any different structure than interfacing a precursor with another hydrogel before forming the second hydrogel, as taught by Morgan (col. 10, lines 33-59). Therefore, it is presumed, absent a showing to the contrary, that the prior art articles of Morgan are the same as or substantially the same as those formed by the product by process limitations that are common technical features of the claims.

8. Because all of the common technical features between groups I and II are disclosed within the prior art, such common technical features cannot be special technical features under PCT Rule 13.2. As a result, the claims corresponding to Groups I and II lack unity of invention.

9. During a telephone conversation with Applicants' representative, Charles Gagnebin, on June 4, 2009, a provisional election was made with traverse to prosecute the invention of Group I, claims 10, 19-20, 24, and 51-54. Affirmation of this election must be made by applicant in replying to this Office action. Claims 31, 39-40, 44, and 55-58 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

10. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

11. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

12. In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

***Priority***

13. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

14. The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

15. The disclosure of the prior-filed application, Application No. 60/505,155, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. With respect to claim 20 and 53, there is no support for the claim limitation directed to a destabilizer contacting the hydrogel and the second hydrogel conforms at least one of the hydrogels to adhere the interfaced hydrogels together when a concentration of the destabilizer is reduced. With respect to claims 24 and 54, there is no support for the claim limitation directed to combining the precursors of the hydrogel and the second hydrogel to interface the hydrogels. With respect to claims 51-53, there is no support for the claim limitations directed to contacting the hydrogels by a flow of a liquid or where the materials of the liquid adhere to a portion of the hydrogels.

***Claim Rejections - 35 USC § 102***

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

17. Claims 10 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Pat. App. Pub. No. 2001/0018612 to Carson et al.

18. With respect to claim 10, Carson discloses a three-dimensional hydrogel structure (ICL 10, paragraph [0026]) micropatterned (having a diffractive surface 18, paragraph [0026]) by a mold (mold, paragraph [0043]) from which the hydrogel structure has been separated (paragraph [0043]), the hydrogel structure comprising: a polymer array of a hydrogel (hydrogel M1, paragraphs [0027]-[0033]), the polymer array comprising a fluid that hydrates the polymer array (M1 has a water content of between 58% and 60%, paragraph [0034]) and a second hydrogel (hydrogel M2, paragraphs [0035]-[0042], M2 is a hydrogel, see abstract/claims) comprising a second polymer array hydrated by a second fluid (M2 has a water content of about 73%, paragraph [0042]); and a micropattern defining a surface of at least one hydrogel (diffractive surface 18, paragraph [0026]), the micropattern corresponding to an inverse micropattern transferred from a mold after separation of the mold from the hydrogels (paragraph [0043]). Therefore, claim 10 is rejected as anticipated by the cited art.

19. With respect to claim 19, Carson discloses a three-dimensional hydrogel structure (ICL 10, paragraph [0026]) micropatterned (having a diffractive surface 18, paragraph [0026]) by a mold (mold, paragraph [0043]) from which the hydrogel structure has been separated (paragraph [0043]), the hydrogel structure comprising: a polymer array of a hydrogel (hydrogel M1, paragraphs [0027]-[0033]), the polymer array comprising a fluid that hydrates the polymer array (M1 has a water content of between 58% and 60%, paragraph [0034]), wherein the hydrogel is interfaced with a precursor of a second hydrogel (pre-cure M2, paragraph [0043]) comprising a second polymer array (hydrogel M2, paragraphs [0035]-[0042], M2 is a hydrogel, see abstract/claims) hydrated by a second fluid (M2 has a water content of about 73%, paragraph [0042]), whereby the precursor of the second hydrogel diffuses into the hydrogel interfaced therewith to adhere the hydrogels as the second hydrogel forms (at least minimal diffusion would inherently have occurred at the boundary between M1 and M2, especially because the materials are bondable, see paragraph [0035]); and a micropattern defining a surface of at least one hydrogel (diffractive surface 18, paragraph [0026]), the micropattern corresponding to an inverse micropattern transferred from a mold after separation of the mold from the hydrogels (paragraph [0043]). Therefore, claim 19 is also rejected.

20. Claims 10 and 19 are rejected under 35 U.S.C. 102(a/e) as being anticipated by U.S. Pat. No. 6,479,072 to Morgan et al.

21. With respect to claim 10, Morgan discloses a three-dimensional hydrogel structure (composite dermal analog, col. 10, lines 33-48) micropatterned by a mold (PDMS negative replicate, col. 9, lines 62 to col.10, line 4) from which the hydrogel (basal lamina analog, col. 9, line 40 to col. 10, line 59) has been separated (dried membrane is peeled from PDMS replicate,

col. 9, lines 62 to col.10, line 4), the hydrogel structure comprising: a polymer array of a hydrogel (cross-linked collagen-GAG dispersion, col. 9, lines 40-62 and col. 10, lines 49-59), the polymer array comprising a fluid that hydrates the polymer array (water/phosphate buffered saline, col. 10, lines 49-59) and a second hydrogel (rehydrated collagen sponge, col. 10, lines 33-59) comprising a second polymer array (cross-linked collagen-GAG dispersion, col. 10, lines 33-59) hydrated by a second fluid (water/phosphate buffered saline, col. 10, lines 49-59) and a micropattern (channels 42, col. 10, lines 5-8) defining a surface of at least one hydrogel (col. 10, lines 5-8) the micropattern corresponding to an inverse micropattern transferred from a mold after separation of the mold from the hydrogels (col. 9, lines 63 to col. 10, line 8). Therefore, claim 10 is rejected as anticipated by the cited art.

22. With respect to claim 19, Morgan discloses a three-dimensional hydrogel structure (composite dermal analog, col. 10, lines 33-48) micropatterned by a mold (PDMS negative replicate, col. 9, lines 62 to col.10, line 4) from which the hydrogel (basal lamina analog, col. 9, line 40 to col. 10, line 59) has been separated (dried membrane is peeled from PDMS replicate, col. 9, lines 62 to col.10, line 4), the hydrogel structure comprising: a polymer array of a hydrogel (cross-linked collagen-GAG dispersion, col. 9, lines 40-62 and col. 10, lines 49-59), the polymer array comprising a fluid that hydrates the polymer array (water/phosphate buffered saline, col. 10, lines 49-59), wherein the hydrogel is interfaced with a precursor (uncrosslinked collagen-GAG dispersion, col. 10, lines 33-48) of a second hydrogel (rehydrated collagen sponge, col. 10, lines 33-59) comprising a second polymer array (cross-linked collagen-GAG dispersion, col. 10, lines 33-59) hydrated by a second fluid (water/phosphate buffered saline, col. 10, lines 49-59), whereby the precursor of the second hydrogel diffuses into the hydrogel

interfaced therewith to adhere the hydrogels as the second hydrogel forms (at least a limited amount of diffusion of a dispersed component would inherently occur where the microfabricated basal analog is floated on the dispersion, because the basal analog is porous and not hydrophobic (it can be hydrated by a dilute acetic acid solution, col. 10, lines 49-59)); and a micropattern (channels 42, col. 10, lines 5-8) defining a surface of at least one hydrogel (col. 10, lines 5-8) the micropattern corresponding to an inverse micropattern transferred from a mold after separation of the mold from the hydrogels (col. 9, lines 63 to col. 10, line 8). Therefore, claim 19 is also rejected.

23. Claim 52 is rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Pat. No. 6,479,072 to Morgan et al.

24. With respect to claim 52, Morgan discloses the three-dimensional hydrogel structure of claim 19, as described with reference to the 35 U.S.C. 102(a/e) rejection of claim 19 as anticipated by Morgan, *supra*, wherein the hydrogel and second hydrogel form a network (composite is covalently cross-linked, col. 10, lines 49-59); the network is contacted by flow of a liquid (col. 11, lines 61 to col. 12, line 13); the liquid comprises materials that are selected from the group consisting of biological components, organic components, metallic components, cellular components, synthetic components, intact cells, inorganic components and combinations thereof (liquid comprises biological/organic/cellular components/intact cells, i.e. cells, col. 11, line 61, to col. 12, line 13); the materials of the liquid adhere to a portion of the network (cells adhere to the surface of the basal lamina, col. 13, lines 8-17); and a portion of at least one hydrogel is interfaced with a substrate (hydrogels are placed on a stainless steel plate, i.e. substrate, col. 12, lines 26-31). Therefore, claim 52 is rejected as anticipated by the cited art.

***Claim Rejections - 35 USC § 102/103***

25. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

26. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

27. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

28. Claims 20, 24, and 54 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over U.S. Pat. App. Pub. No. 2001/0018612 to Carson et al.

29. With respect to claim 20, Carson discloses a three-dimensional hydrogel structure (ICL 10, paragraph [0026]) micropatterned (having a diffractive surface 18, paragraph [0026]) by a mold (mold, paragraph [0043]) from which the hydrogel structure has been separated (paragraph [0043]), the hydrogel structure comprising: a polymer array of a hydrogel (hydrogel M1, paragraphs [0027]-[0033]), the polymer array comprising a fluid that hydrates the polymer array (M1 has a water content of between 58% and 60%, paragraph [0034]), wherein the hydrogel is interfaced (paragraph [0043]) with and a second hydrogel (hydrogel M2, paragraphs [0035]-[0042], M2 is a hydrogel, see abstract/claims) comprising a second polymer array hydrated by a second fluid (M2 has a water content of about 73%, paragraph [0042]); and a micropattern defining a surface of at least one hydrogel (diffractive surface 18, paragraph [0026]), the micropattern corresponding to an inverse micropattern transferred from a mold after separation of the mold from the hydrogels (paragraph [0043]).

30. Carson does not explicitly disclose that a destabilizer contacting the hydrogel and the second hydrogel conforms at least one of the hydrogels to adhere the interfaced hydrogels together when a concentration of the destabilizer is reduced. However, this limitation is a product-by-process limitation. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. See In Re Thorpe, 227 USPQ 964. See MPEP 2113. Absent a showing to the contrary, it is expected that this specific method of adhering the interfaced hydrogels does not confer any structural or

compositional limitations to the claimed article beyond the limitations elsewhere recited in claim 20, and anticipated by Carson. Moreover, there is currently no indication that any different structure would result in the three-dimensional hydrogel structure because the hydrogels were interfaced through the use of a destabilizer to destabilize one of the hydrogels (i.e. causing it to de-gel) and then removing the destabilizer (i.e. allowing the hydrogels to re-gel) as opposed to simply causing one hydrogel to gel while already interfaced with the other hydrogel, as taught by Carson (paragraph [0043]), especially since the character of a de-gelled hydrogel and an ungelled hydrogel precursor would essentially be the same with regard to forming an interface with another gel. Therefore, it is presumed, absent a showing to the contrary, that the prior art articles of Carson are the same as or substantially the same as those formed by the product by process limitations of claim 20. Thus, claim 20 is rejected as either anticipated by or obvious over the cited art.

31. With respect to claim 24, Carson discloses a three-dimensional hydrogel structure (ICL 10, paragraph [0026]) micropatterned (having a diffractive surface 18, paragraph [0026]) by a mold (mold, paragraph [0043]) from which the hydrogel structure has been separated (paragraph [0043]), the hydrogel structure comprising: a polymer array of a hydrogel (hydrogel M1, paragraphs [0027]-[0033]), the polymer array comprising a fluid that hydrates the polymer array (M1 has a water content of between 58% and 60%, paragraph [0034]) and a second hydrogel (hydrogel M2, paragraphs [0035]-[0042], M2 is a hydrogel, see abstract/claims) comprising a second polymer array hydrated by a second fluid (M2 has a water content of about 73%, paragraph [0042]); and a micropattern defining a surface of at least one hydrogel (diffractive

surface 18, paragraph [0026]), the micropattern corresponding to an inverse micropattern transferred from a mold after separation of the mold from the hydrogels (paragraph [0043]).

32. Carson does not explicitly disclose that precursors of the hydrogel and the second hydrogel were combined to interface the hydrogels as at least one hydrogel is formed. However, this limitation is a product-by-process limitation. Absent a showing to the contrary, it is expected that this specific method of interfacing the hydrogels recited herein does not confer any structural or compositional limitations to the claimed article beyond the limitations recited elsewhere in claim 24, and anticipated by Carson. Moreover, there is no indication that that interfacing the precursors of the hydrogels would lead to any different structure than interfacing a precursor with another hydrogel before forming the second hydrogel, as taught by Carson (paragraph [0043]). Therefore, it is presumed, absent a showing to the contrary, that the prior art articles of Carson are the same as or substantially the same as those formed by the product by process limitations of claim 24. Thus, claim 24 is rejected as either anticipated by or obvious over the cited art.

33. With respect to claim 54, Carson discloses that the precursor of the hydrogel or second hydrogel comprises a material selected from the group consisting of biological components, organic components, metallic components, cellular components, synthetic components, intact cells, inorganic components and combinations thereof (precursors comprise at least organic materials, paragraphs [0027]-[0042]). Therefore, claim 54 is also rejected.

34. Claims 20, 24, 51, and 53-54 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over U.S. Pat. No. 6,479,072 to Morgan et al.

35. With respect to claim 51, Morgan discloses the three-dimensional hydrogel structure of claim 10, as described with respect to the 35 U.S.C. 102(a/e) rejection of claim 10 as anticipated by Morgan, *supra*, wherein: the hydrogel comprises a cavity (channels 42, col. 10, lines 5-8); the cavity is contacted by flow of a liquid (col. 11, lines 61 to col. 12, line 13) and the liquid comprises materials that are selected from the group consisting of biological components, organic components, metallic components, cellular components, synthetic components, intact cells, inorganic components and combinations thereof (liquid comprises biological/organic/cellular components/intact cells, i.e. cells, col. 11, line 61, to col. 12, line 13), and further where the materials of the liquid adhere to a portion of the cavity (cells formed stratified epidermal layers covering the cavities, col. 13, lines 8-17); and a portion of at least one hydrogel is interfaced with a substrate (hydrogels are placed on a stainless steel plate, i.e. substrate, col. 12, lines 26-31).

36. Morgan does not explicitly disclose that the cavity is formed by perturbing a portion of the second hydrogel; the portion of the second hydrogel is perturbed by one of a change in temperature or an enzyme digesting the portion; the mold substantially comprises silicon materials, poly (dimethylsiloxane) materials, photoresist materials, glass materials, plastic materials, rubber materials, synthetic materials, polymer materials, organic materials or any combination thereof; the polymer array further comprises materials selected from the group consisting of biological components, organic components, metallic components, cellular components, synthetic components, intact cells, inorganic components and combinations thereof. However, this limitation is a product-by-process limitation. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the

product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. See In Re Thorpe, 227 USPQ 964. See MPEP 2113. Absent a showing to the contrary, it is expected that this specific method of forming a cavity does not confer any structural or compositional limitations to the claimed article beyond the limitations elsewhere recited in claim 52 and in claim 19, and anticipated by Morgan. Moreover, there is currently no indication that the cavity formed by perturbing a portion of the second hydrogel, as claimed, would result in any structure different than directly micropatterning the cavity into the surface of the hydrogel, as taught by Morgan (col. 9, line 63, to col. 10, line 4). Therefore, it is presumed, absent a showing to the contrary, that the prior art articles of Morgan are the same as or substantially the same as those formed by the product by process limitations of claim 52. Thus, claim 52 is rejected as either anticipated by or obvious over the cited art.

37. With respect to claim 20, Morgan discloses a three-dimensional hydrogel structure (composite dermal analog, col. 10, lines 33-48) micropatterned by a mold (PDMS negative replicate, col. 9, lines 62 to col.10, line 4) from which the hydrogel (basal lamina analog, col. 9, line 40 to col. 10, line 59) has been separated (dried membrane is peeled from PDMS replicate, col. 9, lines 62 to col.10, line 4), the hydrogel structure comprising: a polymer array of a hydrogel (cross-linked collagen-GAG dispersion, col. 9, lines 40-62 and col. 10, lines 49-59), the polymer array comprising a fluid that hydrates the polymer array (water/phosphate buffered saline, col. 10, lines 49-59), wherein the hydrogel is interfaced (col. 10, lines 45-59) with a second hydrogel (rehydrated collagen sponge, col. 10, lines 33-59) comprising a second polymer

array (cross-linked collagen-GAG dispersion, col. 10, lines 33-59) hydrated by a second fluid (water/phosphate buffered saline, col. 10, lines 49-59); and a micropattern (channels 42, col. 10, lines 5-8) defining a surface of at least one hydrogel (col. 10, lines 5-8) the micropattern corresponding to an inverse micropattern transferred from a mold after separation of the mold from the hydrogels (col. 9, lines 63 to col. 10, line 8).

38. Morgan does not explicitly disclose that a destabilizer contacting the hydrogel and the second hydrogel conforms at least one of the hydrogels to adhere the interfaced hydrogels together when a concentration of the destabilizer is reduced. However, this limitation is a product-by-process limitation. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. See In Re Thorpe, 227 USPQ 964. See MPEP 2113. Absent a showing to the contrary, it is expected that this specific method of adhering the interfaced hydrogels does not confer any structural or compositional limitations to the claimed article beyond the limitations elsewhere recited in claim 20, and anticipated by Morgan. Moreover, there is currently no indication that any different structure would result in the three-dimensional hydrogel structure because the hydrogels were interfaced through the use of a destabilizer to destabilize one of the hydrogels (i.e. causing it to de-gel) and then removing the destabilizer (i.e. allowing the hydrogels to re-gel) as opposed to simply causing one hydrogel to gel while already interfaced with the other hydrogel, as taught by Morgan (col. 10, lines 33-59), especially since the character of a de-gelled hydrogel and an

ungelled hydrogel precursor would essentially be the same with regard to forming an interface with another gel. Therefore, it is presumed, absent a showing to the contrary, that the prior art articles of Morgan are the same as or substantially the same as those formed by the product by process limitations of claim 20. Thus, claim 20 is rejected as either anticipated by or obvious over the cited art.

39. With respect to claim 53, Morgan discloses that the hydrogel and second hydrogel form a network (composite is covalently cross-linked, col. 10, lines 49-59); the network is contacted by flow of a liquid (col. 11, lines 61 to col. 12, line 13); the liquid comprises materials that are selected from the group consisting of biological components, organic components, metallic components, cellular components, synthetic components, intact cells, inorganic components and combinations thereof (liquid comprises biological/organic/cellular components/intact cells, i.e. cells, col. 11, line 61, to col. 12, line 13); the materials of the liquid adhere to a portion of the network (cells adhere to the surface of the basal lamina, col. 13, lines 8-17); and a portion of at least one hydrogel is interfaced with a substrate (hydrogels are placed on a stainless steel plate, i.e. substrate, col. 12, lines 26-31).

40. Morgan does not explicitly disclose that the destabilizer is selected from the group consisting of chaotropes, kosmotropes, urea, glucose, glycerol, guanidinium hydrogen chloride and combinations thereof; the concentration of the destabilizer is reduced when a stabilizer contacts the hydrogels; the destabilizer and the stabilizer are both selected from the group consisting of chaotropes, kosmotropes, urea, glucose, glycerol, guanidinium hydrogen chloride and combinations thereof. However, as stated previously with respect to claim 20, the recitation of the use of a destabilizer to perturb one hydrogel to interface the hydrogels is a product by

process limitation. Absent a showing to the contrary, it is expected that the additional process limitations recited herein do not confer any structural or compositional limitations to the claimed article beyond the limitations recited elsewhere in claims 53 and 20, and anticipated by Morgan, for at least the reasons set forth above with respect to claim 20. Therefore, it is presumed, absent a showing to the contrary, that the prior art articles of Morgan are the same as or substantially the same as those formed by the product by process limitations of claim 53. Thus, claim 53 is rejected as either anticipated by or obvious over the cited art.

41. With respect to claim 24, Morgan discloses a three-dimensional hydrogel structure (composite dermal analog, col. 10, lines 33-48) micropatterned by a mold (PDMS negative replicate, col. 9, lines 62 to col.10, line 4) from which the hydrogel (basal lamina analog, col. 9, line 40 to col. 10, line 59) has been separated (dried membrane is peeled from PDMS replicate, col. 9, lines 62 to col.10, line 4), the hydrogel structure comprising: a polymer array of a hydrogel (cross-linked collagen-GAG dispersion, col. 9, lines 40-62 and col. 10, lines 49-59), the polymer array comprising a fluid that hydrates the polymer array (water/phosphate buffered saline, col. 10, lines 49-59) and a second hydrogel (rehydrated collagen sponge, col. 10, lines 33-59) comprising a second polymer array (cross-linked collagen-GAG dispersion, col. 10, lines 33-59) hydrated by a second fluid (water/phosphate buffered saline, col. 10, lines 49-59); and a micropattern (channels 42, col. 10, lines 5-8) defining a surface of at least one hydrogel (col. 10, lines 5-8) the micropattern corresponding to an inverse micropattern transferred from a mold after separation of the mold from the hydrogels (col. 9, lines 63 to col. 10, line 8).

42. Morgan does not explicitly disclose that precursors of the hydrogel and the second hydrogel were combined to interface the hydrogels as at least one hydrogel is formed. However,

this limitation is a product-by-process limitation. Absent a showing to the contrary, it is expected that this specific method of interfacing the hydrogels recited herein does not confer any structural or compositional limitations to the claimed article beyond the limitations recited elsewhere in claim 24, and anticipated by Morgan. Moreover, there is no indication that that interfacing the precursors of the hydrogels would lead to any different structure than interfacing a precursor with another hydrogel before forming the second hydrogel, as taught by Morgan (col. 10, lines 33-59). Therefore, it is presumed, absent a showing to the contrary, that the prior art articles of Morgan are the same as or substantially the same as those formed by the product by process limitations of claim 24. Thus, claim 24 is rejected as either anticipated by or obvious over the cited art.

43. With respect to claim 54, Morgan discloses that the precursor of the hydrogel or second hydrogel comprises a material selected from the group consisting of biological components, organic components, metallic components, cellular components, synthetic components, intact cells, inorganic components and combinations thereof( the precursors are biological/organic components, i.e. collagen and glycosaminoglycan, col. 9, lines 40-62 and col. 10, liens 33-48). Therefore, claim 54 is also rejected.

***Conclusion***

44. Any inquiry concerning this communication or earlier communications from the examiner should be directed to NATHAN E. COMSTOCK whose telephone number is (571) 270-1133. The examiner can normally be reached on Monday through Thursday, 8am-5pm Eastern Standard Time.

45. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael LaVilla can be reached on (571) 272-1539. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

46. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/N.E.C./
Nathan E. Comstock
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16 June 2009

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**21 June 2009**